

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ÉTATS-UNIS D'AMÉRIQUE

in its capacity as elected Office

Date of mailing (day/month/year)

24 November 1999 (24.11.99)

International application No.

PCT/US98/26709

Applicant's or agent's file reference

5712-01-MJA

International filing date (day/month/year)

15 December 1998 (15.12.98)

Priority date (day/month/year)

31 March 1998 (31.03.98)

Applicant

DUDLEY, Danette, Andrea et al

1. The designated Office is hereby notified of its election made:



in the demand filed with the International Preliminary Examining Authority on:

12 October 1999 (12.10.99)



in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland

Facsimile No.: (41-22) 740.14.35

Authorized officer

Beatriz Morariu

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

=> Rose Armstrong

5712
PCT

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

Ivo Mansmann/Dr. R. Tesch
Warner-Lambert Company
Legal Division
c/o Gödecke AG
Mooswaldallee 1
D-79090 Freiburg
ALLEMAGNE

Patentwesen

Eing.: - 3. April 2000

PCT

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL PRELIMINARY
EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing
(day/month/year)

3 1. 03. 00

Applicant's or agent's file reference
5712-01-MJA

IMPORTANT NOTIFICATION

International application No.
PCT/US98/26709

International filing date (day/month/year)
15/12/1998

Priority date (day/month/year)
31/03/1998

Applicant

WARNER-LAMBERT COMPANY et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

 European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized officer

Neubauer, M

Tel. +49 89 2399-7272





Express Mail No. EJ881198617US
PD-5712-01-MJA

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 5712-01-MJA		FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US98/26709	International filing date (day/month/year) 15/12/1998	Priority date (day/month/year) 31/03/1998	
International Patent Classification (IPC) or national classification and IPC C07D401/06			
Applicant WARNER-LAMBERT COMPANY et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> I <input checked="" type="checkbox"/> Basis of the report II <input type="checkbox"/> Priority III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability IV <input type="checkbox"/> Lack of unity of invention V <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement VI <input checked="" type="checkbox"/> Certain documents cited VII <input type="checkbox"/> Certain defects in the international application VIII <input checked="" type="checkbox"/> Certain observations on the International application 			
Date of submission of the demand 12/10/1999		Date of completion of this report 31.03.00	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized officer Herz, C Telephone No. +49 89 2399 8275 	

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US98/26709

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-89 as originally filed

Claims, No.:

1-30 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 14-25, 29, 30.

because:

- ☒ the said international application, or the said claims Nos. 14-25, 29, 30 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US98/26709

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims 3-13, 26-28
	No:	Claims 1, 2
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-13, 26-28
Industrial applicability (IA)	Yes:	Claims 1-13, 26-28
	No:	Claims

2. Citations and explanations

see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/US98/26709

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US98/26709

1. The priority documents pertaining to the present application were not available at the time of establishing the first written opinion. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct document DE-A-197 18 181 cited in the International Search Report could become relevant in order to assess whether the claims satisfy the criteria set forth in Article 33 (1) PCT.

2. Claims 14-25, 29, and 30 are directed to a therapeutical method performed on humans. Under the terms of Rule 67.1 (iv) PCT, the International Preliminary Examination Authority is not required to carry out an examination on such claim.

3. The subject-matter claimed in the present application is anticipated by the disclosure of the documents classified "X" in the International Search Report (ISER). Hence, the subject-matter claimed in Claims 1 and 2 is considered not to be new under 33 (2) PCT and the Applicant is requested to delimit these claims accordingly.

With regard to the presence of inventive step reference is made to the documents classified "Y" and "Y" in the ISER wherein similar compounds possessing the presently claimed pharmacological activities have been disclosed. Substituents therein are the same as or similar to those given in the present application.

Taking into account these facts the man skilled in the art would have to expect the desired pharmacological activities without affecting their basic capabilities when modifying the basic moiety and/or the substituents of the groups of compounds disclosed in the state of the art. Thus representing only predictable effects the compounds claimed are considered to be obvious.

Consequently, Claims 1-13 and 26-28 are also lacking inventive step under Article 33 (3) PCT.

4. The use of the terms "pharmaceutically acceptable esters, amides, or prodrugs; alkyl; aryl; hetero; aldehyde; ketone; acid; ester" and their compositions throughout the claims without further definitive qualification therein renders these claims obscure in scope in that it does not indicate any specific substituents. As chemical species can be precisely defined by the identity and number of atoms involved (cf. the definitions given on pages 39 to 43) the above terms are considered to render these claims obscure in scope in that it does not indicate any specific substituents. Therefore it is not clear whether the compounds implied fall within the scope of the claims of the present application and/or constitute a solution to the problem underlying the application; the incorporation of the specific substituents given in the specification is therefore necessary (Articles 6, 33 (3) PCT).

NOTED

PATENT COOPERATION TREATY

JUN - 8 1999

R. ARMSTRONG
From the INTERNATIONAL SEARCHING AUTHORITY

To:
WARNER-LAMBERT COMPANY
Attn. RYAN, A.
201 Tabor Road
Morris Plains, New Jersey 07950
UNITED STATES OF AMERICA

RECEIVED

NOTIFICATION OF TRANSMITTAL OF
THE INTERNATIONAL SEARCH REPORT
OR THE DECLARATION

MP PATENT DEPT
(PCT Rule 44.1)

Date of mailing
(day/month/year)

04.06.99

Applicant's or agent's file reference

5712-01-MJA

FOR FURTHER ACTION

See paragraphs 1 and 4 below

International application No.

PCT/US 98/26709

International filing date
(day/month/year)

15/12/1998

Applicant

WARNER-LAMBERT COMPANY et al.

1. ☒ The applicant is hereby notified that the International Search Report has been established and is transmitted herewith.

Filing of amendments and statement under Article 19:

The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

Where? Directly to the International Bureau of WIPO
34, chemin des Colombettes
1211 Geneva 20, Switzerland
Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2. ☐ The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3. ☐ **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

☐ the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

☐ no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication.

Within **19 months** from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within **20 months** from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the International Searching Authority



European Patent Office, P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Wolfgang Borinski

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 5712-01-MJA	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US 98/ 26709	International filing date (day/month/year) 15/12/1998	(Earliest) Priority Date (day/month/year) 31/03/1998
Applicant WARNER-LAMBERT COMPANY et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☒ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

QUINOLONES AS SERINE PROTEASE INHIBITORS

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

//////

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US 98/26709

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.: 1, 2, 14-25, 29, 30
because they relate to subject matter not required to be searched by this Authority, namely:
Claims 14-25, 29 and 30 are directed to a therapeutical method performed on humans. Under the terms of Article 17 (2) (b) PCT, Rule 39 (1) (iv), the International Search Authority is not required to carry out a search on such claims.
2. ☒ Claims Nos.: 1, 2
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Claims Nos.: 1,2

Claims 1 and 2 were found unsearchable because of the multitude of variables and their permutations and combinations (e. g. A, B, D, E, F, G, K, L, X) result in claims that are so broad that they are rendered virtually incomprehensible and thus, no meaningful search can be given. Therefore, the first discernable subject matter as found in Claims 3 to 13 (i. e. those compounds possessing a quinolone core and a defined nitrogen substituent) has been searched. Claims 1 and 2 have been searched to the extent they encompass the subject matter of Claims 3 to 13. It is further noted that certain substituent definitions do not make any chemical sense (e. g. what is the structure of compounds wherein G, J and K are all absent? what is a monovalent "ketone" substituent L? what is encompassed by an "acid" or "ester"?; etc.).

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/26709

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C07D401/06 C07D401/14 C07D409/14 C07D407/14 C07D413/14
 C07D403/06 A61K31/44 A61K31/47

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C07D A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	F. RICHTER: "Beilsteins Handbuch der Organischen Chemie, 4. Aufl., 1. EW, 20., 21. und 22. Bd." 1935, VERLAG VON JULIUS SPRINGER, BERLIN XP002102648 * 1-Methyl-2-oxo-1.2.3.4-tetrahydro-chinolin * see page 293 ---	1,2
X	F. RICHTER: "Beilsteins Handbuch der Organischen Chemie, 4. Aufl., 20. Bd." 1935, VERLAG VON JULIUS SPRINGER, BERLIN XP002102649 * P. 264: N-Methyl-tetrahydrochinolin; p. 267: N-Benzyltetrahydrochinolin * --- -/--	1

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

12 May 1999

Date of mailing of the international search report

04.06.99

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
 NL - 2280 HV Rijswijk
 Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
 Fax: (+31-70) 340-3016

Authorized officer

Herz, C

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 98/26709

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No
P,Y	DE 197 18 181 A (BOEHRINGER INGELHEIM PHARMA KG) 5 November 1998 see claims 1-10 ----	1-30
Y	JP 50 142576 A (OTSUKA PHARMACEUTICAL CO., LTD.) 17 November 1975 * entire document * ----	1-30
Y	US 4 329 347 A (E. MÜLLER ET AL.) 11 May 1982 see claims 1-9 ----	1-30
Y	FR 2 439 196 A (YOSHITOMI PHARMACEUTICAL IND., LTD.) 16 May 1980 see claims 1-16 ----	1-30
Y	WO 97 12869 A (OTSUKA PHARMACEUTICAL CO., LTD.) 10 April 1997 see claims 1-29 ----	1-30
Y	DE 25 59 509 A (OTSUKA PHARMACEUTICAL CO., LTD.) 30 December 1976 see claims 1-13 -----	1-30

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 98/26709

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
DE 19718181 A	05-11-1998	NONE	
JP 50142576 A	17-11-1975	JP 934278 C JP 53010989 B	30-11-1978 18-04-1978
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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 5712-01-MJA	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/US98/26709	International filing date (day/month/year) 15/12/1998	Priority date (day/month/year) 31/03/1998
International Patent Classification (IPC) or national classification and IPC C07D401/06		
Applicant WARNER-LAMBERT COMPANY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 5 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 12/10/1999	Date of completion of this report 31.03.00
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Herz, C Telephone No. +49 89 2399 8275 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/US98/26709

I. Basis of the report

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

Description, pages:

1-89 as originally filed

Claims, No.:

1-30 as originally filed

2. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

3. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 14-25, 29, 30.

because:

- ☒ the said international application, or the said claims Nos. 14-25, 29, 30 relate to the following subject matter which does not require an international preliminary examination (*specify*):

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International application No. PCT/US98/26709

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 3-13, 26-28
	No: Claims 1, 2
Inventive step (IS)	Yes: Claims
	No: Claims 1-13, 26-28
Industrial applicability (IA)	Yes: Claims 1-13, 26-28
	No: Claims

2. Citations and explanations

see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

**INTERNATIONAL PRELIMINARY
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VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/US98/26709

1. The priority documents pertaining to the present application were not available at the time of establishing the first written opinion. Hence, it is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. If it later turns out that this is not correct document DE-A-197 18 181 cited in the International Search Report could become relevant in order to assess whether the claims satisfy the criteria set forth in Article 33 (1) PCT.
2. Claims 14-25, 29, and 30 are directed to a therapeutical method performed on humans. Under the terms of Rule 67.1 (iv) PCT, the International Preliminary Examination Authority is not required to carry out an examination on such claim.
3. The subject-matter claimed in the present application is anticipated by the disclosure of the documents classified "X" in the International Search Report (ISER). Hence, the subject-matter claimed in Claims 1 and 2 is considered not to be new under 33 (2) PCT and the Applicant is requested to delimit these claims accordingly.

With regard to the presence of inventive step reference is made to the documents classified "Y" and "Y" in the ISER wherein similar compounds possessing the presently claimed pharmacological activities have been disclosed. Substituents therein are the same as or similar to those given in the present application.

Taking into account these facts the man skilled in the art would have to expect the desired pharmacological activities without affecting their basic capabilities when modifying the basic moiety and/or the substituents of the groups of compounds disclosed in the state of the art. Thus representing only predictable effects the compounds claimed are considered to be obvious.

Consequently, Claims 1-13 and 26-28 are also lacking inventive step under Article 33 (3) PCT.

4. The use of the terms "pharmaceutically acceptable esters, amides, or prodrugs; alkyl; aryl; hetero; aldehyde; ketone; acid; ester" and their compositions throughout the claims without further definitive qualification therein renders these claims obscure in scope in that it does not indicate any specific substituents. As chemical species can be precisely defined by the identity and number of atoms involved (cf. the definitions given on pages 39 to 43) the above terms are considered to render these claims obscure in scope in that it does not indicate any specific substituents. Therefore it is not clear whether the compounds implied fall within the scope of the claims of the present application and/or constitute a solution to the problem underlying the application; the incorporation of the specific substituents given in the specification is therefore necessary (Articles 6, 33 (3) PCT).